IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No. :	**WARF-0002**
Inventors:	**Laughon, Allen S.**
Serial No. :	**09/810,385**
Filing Date:	**March 16, 2001**
Examiner:	**Harris, Alana M.**
Customer No. :	**26259**
Group Art Unit:	**1643**
Confirmation No. :	**8778**
Title:	**Compositions and Methods for Negative Regulation of TGF-ß Pathways**

Express Mail Label No. EV794825581US
Date of Deposit ~~December 12, 2~~005

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RULE 132 DECLARATION

1. I, Dr. Allen S. Laughon, Ph.D. am the inventor in U.S. Patent Application Serial No. 09/810,385 filed March 16, 2001 and am most familiar with the subject matter of this application and the research effort which lead to the discovery of the instant invention.

2. As described in the '385 application at pages 14 and 15, a cell-based reporter assay has been used to identify compounds that interfere with transcriptional repression of genes induced by a TGF-ß, activin or bone morphogenetic protein signal in cells. The components

used in the assay were known at the time of filing of the '385 application and are those described in the '385 application and depicted in Figure 6, namely Mad and Medea as Smad proteins, Shn as the DNA-binding Smad co-repressor protein, dCtBP, and lacZ as the reporter, the expression of which is controlled by the *brk* promoter, a direct target of Mad/Medea and Schnurri (see abstract of Muller et al. (2003) *Cell* 113:221– 233; Exhibit A).

The results of this assay (see Exhibit B) show that a mutant version of the adenovirus E1A protein (designated in Exhibit B as pPACE1A), which is a documented inhibitor of CtBP, blocks repression of the *brk–lacZ* reporter construct in transiently transfected Drosophila S2 cells. In this assay, repression of the *brk–lacZ* reporter is caused by cotransfection of a plasmid that expresses TkvQD, an activated form of the type I Dpp receptor. Cotransfection with a plasmid expressing E1A blocks this repression by inhibiting CtBP. Accordingly, having used the well-known assay components and guidance provided in the specification for carrying out the method of the '385 application, we have successfully identified a compound that interferes with transcriptional repression of genes induced by a TGF-13, activin or bone morphogenetic protein signal in cells.

I hereby declare that all statements herein of our own knowledge are true and that all statements made on information or belief are believed to be true; and further that these statements were made with the knowledge that willful statements and the like so made are punishable by fine or by imprisonment, or both under §1001 of Title 18 or the United States Code, and that such willful statements may jeopardize the validity of the application, any patent issuing there upon, or any patent to which this verified statement is directed.

Dr. Allen S. Laughon, Ph.D.

Date: Dec. 9, 2005